Submitter Name: Benjamin H. Grissom Submitter Email: Bgrissom@som.umaryland.edu
PI Name: Seth A. Ament PI Email: Sament@som.umaryland.edu

A single-cell multi-omic atlas of the ventral pallidum reveals VGLUT1 neuron-specific transcriptional responses in immediate and prolonged forced abstinence from heroin self-administration

Benjamin Grissom[1], Marcia Cortes-Gutierrez[1], Swarup Mitra[2], Rianne Campbell[1], Bareera Qamar[1], Seth A. Ament[1]*, David M. Dietz[2]*, and Mary Kay Lobo[1]*

[1]University of Maryland School of Medicine;
[2]University at Buffalo, Jacobs School of Medicine and Biomedical Sciences

Opioid addiction is associated with long term changes in the ventral pallidum (VP), a ventral basal ganglia component of the mesolimbic dopamine reward system, yet the cell type diversity in the VP and the molecular adaptations associated with substance use and addiction are poorly understood. Here, we produced a single-nuclei transcriptome and chromatin accessibility atlas for the cell types of the rat VP in the context of heroin self-administration and forced abstinence. We identified 48 transcriptionally distinct neuronal subtypes, including multiple GABAergic, glutamatergic, and cholinergic sub-classes. Heroin self-administration was associated with prominent transcriptional changes in VGLUT1-expressing neurons, including the transcriptional upregulation of several glutamate receptor components, accompanied by downregulation of a GABA receptor subunit, *Gabrg1*. Heroin self-administration was also associated with transcriptional changes in in non-neuronal cells, including dysregulation of cell adhesion and restructuring genes in oligodendrocytes and oligodendrocyte precursor cells. Many of these acute effects of heroin were diminished after 14 days of forced abstinence, while we observed persistent effects on the expression of genes involved in prostaglandin signaling and related inflammatory processes. Our results provide insight into the gene regulatory mechanisms mediating the acute and persistent effects of opioids on the brain.